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Advances in Magnetic Nanoparticles for Biomedical Applications

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ABSTRACT

Magnetic nanoparticles have emerged as an extensive array of functional nanomaterials with unique chemical and physical characteristics. The physical background of these magnetic nanoparticles lies in the interaction with an external magnetic field. Magnetic nanoparticles (MNPs), when used in conjunction with an external magnetic field and magnetizable grafts, allow particles to be delivered to a specific target region, fixed at the local site while the drug is released, and acted locally. Magnetic nanoparticles (MNPs) have gained much attention due to their unique properties that are extremely useful in therapeutic fields such as MRI, drug delivery, heat, magnetic particle imaging (MPI), and contrast enhancement agents. The current study includes a short description of biomagnetic nanostructures, magnetic nanoparticle production techniques, and biomedical applications. Finally, a future view of magnetic nanoparticles in biomedicine is also discussed.

Keywords: Magnetic Nanoparticles; Biomedical Engineering; Biomedical Applications

Abbreviations: MRI: Magnetic Resonance Imaging; MPI: Magnetic Particle Imaging; BMNPs: Bio-Magnetic Nanoparticles; ZA: Zolendronic Acid; INS: Infrared Neural Stimulation; PVA: Polyvinyl Alcohol; CLIO: Cross-Linked Iron Oxide; PEG: Polyethylene Glycol

Introduction

Magnetic nanoparticles (MNPs) have received a lot of interest recently because of their unique characteristics that are highly beneficial in the clinical field including magnetic resonance imaging (MRI), drug delivery, hyperthermia, magnetic particle imaging (MPI), and contrast enhancement agents [1]. MNPs, which have nano-dimensions, have been effectively coupled to chemotherapeutic drugs and the fragment antigen-binding domains of antibodies to improve MNP targeting and therapeutic efficacy [2]. MNPs are composed of magnetic elements such as Fe, Cr, Gd, Co, Mn, and Ni, as well as corresponding chemical substances such as alloys, oxides, and ferrites [3]. These MNPs, which have magnetic properties, thus follow Coulomb's law of electrostatic force interactions, allowing the particles to be controlled using a magnetic field [2]. Among the above mentioned MNPs, Fe2O3 and Fe3O4 are the most commonly used MNPs due to their low toxicity. In light of the fact that magnetic nanoparticles can exhibit a variety of unusual characteristics such as high magnetic field, superparamagnetism, and anisotropy, these characteristics determine specific biomedical applications. From the various MNPs that have been developed, those that exhibit rapid magnetic state changes upon application of an external field

and no remanence at RT (superparamagnetism) are the ones that are desired usually [4]. It is important to keep in mind that long-term storage of synthesized MNPs leads to their instability and agglomeration. This results in the reduction of energy associated with nanoparticles' high surface-to-volume ration and limits their use in biomedical applications. Numerous surface modification methods have been developed to reduce the agglomeration and surface functionalization which are necessary to ensure stability [5]. Surface modification of magnetic nanoparticles is done utilizing different polymer systems that make the material utilized in vivo more biocompatible and biodistributive.

Multifunctional coatings have been introduced using molecular functionalization techniques in order to allow these magnetic particles to be used for diagnostic, imaging, and therapeutic purposes [6]. Nanotechnology has gained eminence in technological advancement because of its uniquely tunable physicochemical properties such as light absorption, catalytic activity, wettability, thermal and electrical conductivity, and melting point which demonstrated superior performance than its bulk materials. Nanomaterials and nanostructures constitute an active field of study and a long-term socio industry with maximum concentration in several application sectors [7,8].

Bio Magnetic Nanoparticles

Recently, there has been increasing interest in MNPs, with academic and commercial sectors in the pharmaceutical, environmental, and healthcare fields that drawing attention. The primary emphasis of researchers in the biotechnology areas has been on bio-magnetic nanoparticles (BMNPs) (1 to 100 nm ranges). BMNPs' unique chemical process combined with their entirely biocompatible nature make them effective in detecting and diagnosing carcinogenic lesions by targeting drugs as treatment agents at the same time in certain applications [9]. These magnetic biomaterials produce heat in a tissue area when exposed to a magnetic field. Cellulose cancer is destroyed above 43 degrees Celsius, and at this temperature the normal cells might remain. The heat cannot be avoided because of the poor circulatory system formation in the diseased tissue, resulting in a higher temperature than normal tissues around it [10]. The heat cannot be dispersed because the vascular system has poorly developed, and the temperature is much greater than in normal cells. Hyperthermia was therefore seen as an efficient way of treating malignant bone disease without harming normal tissue. Thus, biomagnetic nanoparticles are considered a potential material for hyperthermia treatment and other biomedical applications [10].

Bio Magnetic Nanoparticle Biomedical Applications

Biomagnetic nanoparticles have been extensively studied for their biomedical applications including diagnosis and therapy of infectious diseases and cancer in conjunction with enhancing tissue engineering technologies [2]. Effective biomagnetic nanoparticles depend on size, magnetic characteristics, stability, surface chemistry, and toxicity for diverse biomedical applications. Presently, major research is been carried out in targeted drug delivery to fight against cancer. BMNPs are considered a potential material that have been functionalized with appropriate agents such as PMMA or PEG and other biomolecules. Paclitaxel, doxorubicin, carboplatin and 5-fluorouracil drugs are loaded with BMNPs, aiming at and concentrating especially on tumors via the implementation of external magnetic fields [11] (Hou CH, et al. [12]) performed magnetic hydroxyapatite nanoparticles with in vivo cancer hyperthermia utilizing the mouse model. The magnetic nanoparticles of hydroxyapatite are produced by adding Fe2+ using the co-precipitation method. To carry out the hypothermia, the prepared material was injected into mice around the tumor site and placed into inductive heater with high frequency by altering the magnetic field. In the observation period of 15 days, the dramatic reduction of tumor volume was noted. In addition, the blood test indicated a high biocompatibility with reduced toxicity of the magnetic nano hap material. This shows that new magnetic hydroxyapatite nanoparticles are efficient in the less hazardous mouse model for hyperthermia therapy [12]. In another study, (Seyfoori A, et al. [13]) reported the co-precipitation synthesis of a multifunctional magnetic Hap-ZnFe2O4 nanocomposite. The cytocombatibility study was carried out for the prepared nanocomposite using G-292 and HEK cells. The MTT findings indicated that there was no toxicity on the cells, and that increasing the concentration of nanocomposites enhanced and reduced cell proliferation of G-292 and HEK cells, respectively. In addition, the antibacterial activity of the prepared nanocomposite was studied against the gram-positive bacteria S. aureus and resulted in significant inhibition of bacterial growth. The zolendronic acid (ZA) was added to the Hap-ZnFe2O4 nanocomposite, which serves as a bone anti-cancer biophosphate agent that inhibits osteosarcoma cell growth. The in vitro drug release studies of ZA loaded Hap-ZnFe2O4 nanocomposite revealed the burst release of drug for first 20h followed by slow release until 170h. The outcomes of the study showed that the developed multifunctional biomagnetic nanoparticles may be employed for targeted anticancer medication delivery as well as bacterial growth inhibition following surgeries [13].

Bio-Magnetic Nanoparticles

Without a coating, MNPs have hydrophobic surfaces with large surface area to volume ratios and a propensity to agglomerate [14]. A proper surface coating allows MNPs to be dispersed into homogenous fluids and improve MNP stability. Several groups of coating materials are used to modify MNP surface chemistry.

A few of them are organic polymers such as dextran, chitosan, polyethylene glycol, polylobate, polyaniline, organic surfactants such as sodium oleate and dodecyl amine, inorganic metals such as gold, inorganic oxides such as silica and carbon, bioactive molecules and structures such as liposomes, peptides, and ligands/receptors.

Organic

The medical arrangements for MNPs are traditionally dependent on the organic biodegradable dextran and carbohydrate derivatives because their common use as plasma amplifiers with high affinities for iron Ferridex, Resovist, Combidex, and AMI-288 / ferumoxytol have also been used successfully as comparative MRI agents [15]. By creating a steric repulsion, polymers stabilize MNPs in suspension. But polymer-coated. MNPs are not stable at high temperatures and are not suitable to protect active MNPs from air movement and exposure leakage in acidic conditions [14]. Not working as well as the bonding capacity of polymer-coated MNPs [16] limits their use in sophisticated, integrated applications. However, amination or dextran carboxylation resulting in cross-linked iron oxide MNPs (CLIO) improves their integration capacity. For example, CLIO combined with a fluorescent probe is used successfully in αvβ3 integrin, cathepsin B, E-selectin, VCAM-1, macrophage specific, and other molecular imaging ligands of cells. Polyethylene glycol (PEG) is a polymer widely used for its hydrophilicity and low antigenicity. In addition to the steric stabilization of MNPs, PEG inhibits plasma formation and is engulfed by macrophages, increasing MNP's circulation in vivo [17]. MNPs with PEG-coated cellular infiltration can be improved by fluid-phase endocytosis as well by using amphiphilic affinity to lipid bilayers in plasma membranes [18]. These attributes, however, increase their overload capacity cells which are made of iron and are toxic. Polyvinyl alcohol (PVA) is excellent for film formulation, containing emulsifying and adhesive properties. While the use of PVA in intravenous delivery is limited due to persistence and agglomeration parameters in ferrofluid [19], when cross-linked to create a magnetic gel, PVA can instead be used as a vitreous eye [20]. Where possible, this structure can be used in the direction of drug delivery, tissue engineering, and biosensor technology [19]. Chitosan is an adhesive polymer with natural, biocompatible, cationic, and hydrophilic properties, suitable for the purification of protein and magnetic bioseparation [19]. Interestingly, the labeling of fibroblasts with MNPs associated with chitosan improve their ground attack capacity of magnetic fields, which reflects the promise in applications of tissue engineering [21].

Inorganic

Precious metals, such as gold, have been used to protect iron oxide cores against oxidation as they form very stable, low-level particles [22,23]. Nanogold is known for its high optical properties, biocompatibility, and outstanding performance power [22,23]. One limit is that the addition of gold could weaken the magnetic properties of iron oxide MNPs [24] and is considered difficult to achieve due to the different nature of its two phases [25,23]. When achieved, gold-based MNPs are stable under neutral and sour conditions [26,27]. Continuous engineering of the gold shell on the back of the MNPs is a challenge, but it can provide a very effective barrier against oxidizing agents [19]. Inverted silica shells of various sizes are used to mend the MNPs at different levels of dipole coupling (i.e., direct magnetism dipole-dipole interaction) and magnetic flux coupling. Based on the negative charge of the silica shell, MNPs mixed with silica are dispersed and stable in wet conditions [25]. They give good controlling particle interactions both in solutions and internal structures by varying the strength of the shell [25]. In their manufacturing protocol, the MNP's list of silica-coated iron oxide are in sizes ranging from 1-2 nm [28] to 150 nm [29], but improving monodispersed solutions often seem difficult. MNPs are covered with silica. They have longer cycle times, and their hydrophilic surface has a negative charge providing the appropriate anchorage for the binding of the ligands to introduce an excellent platform for drug delivery [19].

Synthesis Methods

As a multifunctional nanostructured material, biomagnetic nanoparticles exhibit unique physical, chemical, and biological characteristics as well as a variety of applications ranging from various sectors to medical domains [9]. MNPs such as Ni, Co, Fe, Mg, Mn, oxides like Fe2O3 and Fe3O4, and alloys such as CoPt and FePt have been synthesized in various compositions and phases. Different techniques have been reported for the synthesis of magnetic nanoparticles; co-precipitation, microemulsion, and sol-gel synthesis are the most commonly used methods for the synthesis [11].

Co-Precipitation

Co-precipitation is the most commonly used and most appropriate technique for the production of MNPs with regulated sizes and magnetic characteristics. Because of its simplicity of use and lack of hazardous ingredients and methods, it is widely utilized in biomedical applications. MNPs are made from aqueous salt solutions by adding a base in an inert environment at ambient temperature or at elevated temperature in this technique [30]. Mohammadi H. et al. synthesized magnetic nanoparticles by the co-precipitation method and coated with polymeric (PEG), organic (Oleic acid) and inorganic (SiO2) compounds and evaluated the cytotoxicity of the prepared nanoparticles using a MTT assay. The cytotoxicity results revealed that Oleic acid and silica coated magnetic nanoparticles exhibited low toxicity compared to PEG coated nanoparticles. It was well observed from the results that the given dose range between 10 and 40 µg/µl are more suitable for biomedical applications, whereas increasing the dose increased

the cytotoxicity. As a result of these studies, these magnetic nanoparticles are ideal for MRI applications. This research will be used in future investigations in various biomedical applications [31].

Microemulsion

The microemulsion technique for synthesis of nanoparticles is a hot topic right now. Microemulsions have grown in importance both in fundamental research and in a variety of industrial sectors since their discovery. This approach is based on two immiscible water and oil phases under the presence of surfactant. At the oil-water interface, surfactant molecules can form a monolayer, with hydrophilic heads in aqueous phase and hydrophobic tails dissolved in the oil phase [30]. (Kekalo K, et al. [32]) synthesized Iron core/ Iron oxide shell magnetic nanoparticles using the microemulsion method with CTAB and butanol as surfactants and reported their physicochemical properties. Using gradual, controlled oxidation at room temperature, a thin Fe3O4 layer was formed on the iron nanoparticles, and 3-aminopropyltrimethoxysilane was used to form a silica shell on Fe3O4. In an inert environment or even in air, Fe core/ Fe oxide shell nanoparticles maintain their magnetic and physicochemical properties for at least 3 days [32]. (Pham X N, et al. [33]) prepared curcumin loaded magnetic nanoparticles coated with chitosan using a reverse-microemulsion method and studied their application in cancer. The prepared Fe oxide nanoparticles exhibited spherical shapes with sizes ranging from 8 to 17nm. The VSM studies revealed the superparamagnetic nature of the prepared material. Furthermore, the in vitro drug loading demonstrates fast curcumin adsorption during the first stage, followed by a gradual reduction in the drug absorption rate after a period of time. The drug release studies revealed that the presence of soluble phenolic acids and low chitosan concentrations resulted in a slow release rate of the loaded drug. Moreover, the modified nanoparticles' cytotoxicity was found to have anticancer efficacy against A549 cells, with an IC50 value of 73.03 g/ml. As a result, the prepared curcumin loaded, chitosan modified, Fe oxide nanoparticles can be utilized as on-target drug delivery carriers in cancer cell therapy [33].

Sol-Gel Method

The sol-gel technique is an excellent wet approach for producing nanostructured metal oxides. The hydroxylation and condensation of chemical precursors in solution, resulting in a "sol" of nanometric particles, is the basis for this technique. Wet gel is a three-dimensional metal oxide network formed by further condensation and inorganic polymerization. To get the ultimate crystalline state, further heat treatments are required [30]. Metal alkoxides are hydrolyzed and then condensed in the sol-gel method. Metal alkoxides are useful precursors because they can withstand hydrolysis, in which an alkoxide is replaced with a hydroxide group and free alcohol is produced. Precursors, pH, solvent types, catalysts, additives, and temperature are all factors to consider in a sol-gel process. The kinetics, growth, and hydrolysis and condensation processes can all be affected by these variables [30]. Caglar B. et al. reported the synthesis of ferromagnetic BiFeO3 by using the sol-gel method. In their study, for the first time, a new amperometric biosensor based on Cress peroxidase encapsulated on BiFeO3 nanoparticles modified carbon paste electrode was developed to detect H2O2. The peroxidase was extracted from Cress (Lepidium sativum) using ammonium sulphate precipitation and chromatographic methods. Under ideal circumstances, the proposed biosensor showed a linear response to H2O2 in the detection limit of 2.0 107 to 1.0 105 M, and the limit of detection and quantification were estimated. Furthermore, the H2O2 biosensor demonstrated good stability over a ten-day period. Finally, the constructed sensor was utilized to analyze H2O2 in milk samples, yielding good results under the working circumstances [34]. In another study, (Satvekar R K, et al. [35]) developed a novel strategy for fabricating a Silica/Chitosan/Fe3O4 nanocomposite for the biosensing of hydrogen peroxide. The large surface area and porous architecture of a nanocomposite allowed for a significant amount of enzyme to be loaded, and the immobilized enzyme retained its biofunctionality. Furthermore, without the use of a mediator, the Silica/Chitosan/Fe3O4 showed electro-catalytic activity in the reduction of H2O2. Excellent sensitivity, selectivity, repeatability, and stability long term are all features of the sensor. Therefore the developed material has the potential to be useful in third generation electrochemical biosensors [35].

Application of Magnetic Nanoparticles in Biomedicine

MRI Contrast Agents

Iron oxide based nanoparticles have very good optical properties to support the MRI based diagnostics to get a clear image with the enhanced contrast of the nanoparticle [36]. Similar to the iron oxide based contrast agents, there have been various other nanoparticles such as ferumoxides, ferumoxtran, and ferucarbotran used as contrast agents, and they all have been clinically approved to be used in MRI [37]. Nanoparticles have been more useful in MRI when they are used to detect lymph node metastases from solid tumors [38]. Most of the classification from the tumors and metastases identifying the angiogenesis to map the arteries is done with the help of the magnetic nanoparticles [15,39]. Detecting inflammatory pathologies such as atherosclerosis, multiple sclerosis and rheumatoid arthritis was done with the magnetic nanoparticles using the labelling procedure [15,39,40]. CNS regeneration for cell tracking and neuroprotective glia (Schwann cells and olfactory unsheathing cells) is done with the stem cell labelled magnetic nanoparticles [41,42]. Diagnosis of gliomas in post-surgery is done

using the MRI when FITC conjugated MNP's are used as fluorescent markers due to the possibility of the change in the place of gliomas after surgery [39,43-45]. Similarly, identifying the T cells from TAT peptide of HIV is done with the very low dimensional iron oxide MNP's within 5 minutes using the labelling technique [46]. Real time visualization of the tumors is done with the iron oxide MNPs of 2 nm core dimensions, which reveals utmost localization. Similar magnetic nanoparticles are not only used as contrast agents, but can also be used as drug and genetic delivery carriers which reached the site with the guided magnetic field externally [47].

Drug Delivery

Drug delivery to a localized site of the pathological areas with the help of the external control is done with the help of the low dimensional structures carrying the drug to deliver at the sites. MNPs are used as carriers to deliver the drugs to the localized sites with the external control using a magnetic field for the treatment of cancer. It has been an effective and easy method to help cancer patients without any discomfort [48,49]. Further investigation on the MNP based gene and drug delivery method has revealed a new method of treatment for most neurological disorders to the whole blood-brain barrier [50,51]. If the possibility of better linkage between the MNPs, capillaries, external magnetic field, and the pathological domain is accomplished, there would be great progress on the MNP based drug delivery for neurological disorders [19,48]. MNPs that are hydrophilic and less than 100 nm are recommended for drug delivery applications since most of the human system is made with liquid, thus having easy access and delivery to the pathological site [48,52,53].

Tissue Engineering

MNPs work well in tissue engineering application due to their improved physical properties which can be used in the treatment of stem cell replacement therapy in cell labeling, filtering, monitoring, installation, and targeting in vivo delivery [41]. Protein denaturation and re-polymerization of adjacent proteins chains can be done with the MNPs due to their ability to weld joint tissues below high temperatures [54,19]. When MNPs' sensitivity is increased this allows for the selection of light sources for nano-magnetic welding with the gold and silica wear through minimal muscle damage [53-55]. Harvesting multilayered keratinocyte-like 3-D sheets and assembled nanowire arrays using MNPs are used in tissue engineering applications [36,56].

Theragnosis

A therapeutic and diagnostic (theragnostic) approach is adopted to allow the medicine to be used for both the applications with some level of customization [57]. Due to the ability of the MNPs controlled by external magnetic field and their capability to be used as a drug delivery system and also to check the cells on labelling, identifying the parts with the fluorescence nature is widely used on theragnosis applications. Integrated genetic diagnosis and delivery for some type of tumors has been done by some research groups [47]. Similarly, MRI assisted diagnosis and surgery with the help of MNPs has been used with the flexibility of the absence of the magnetic nature in the MNPs when the magnetic field is removed on applications such as MRI directed cell replacement and MRI assisted surgery [43-44,58].

Cell Labelling

Cell labelling manages cell interactions which are significant in the development of the multicellular organisms based on the direct interactions between the cells. Citrate-coated ultra-small MNPs are used to stop the alter viability, function in proliferation, or differentiate cells [59]. This method is mostly used in stem cells due to its regenerative ability to repair itself, the injured, or diseased tissues and organs. Since cell labelling of stem cells should conserve their self-renewal and multipotency after internalization of magnetic nanoparticles, it is more cumbersome and tedious [60,61]. To achieve stability on the cell labelling it is very important to have a good stable magnetic nanoparticle to get differentiation capable magnetism in the process [62]. Co-incubation of cells with magnetic nanoparticles is very useful due the initialization of the particles through the spontaneous endocytosis or phagocytosis pathway. The interaction of nanoparticles based on their property with cells vividly influence in behaviour of cell labelling [63]. MNPs have exciting potential in cell imaging and cell therapy helping in control over cell labelling when compared to other materials as they are simple, rapid, and predictable [64]. Preserving cell behaviour and monitoring cell migration is very important in cell therapy where cell labelling leads to graft imaging, tissue engineering, and magnetic force assisted cell therapy [65,66].

Biosensors

A biosensor is an analytical device that convert a biological response into an electrical signal. Biosensors are highly specific, independent, and reusable with physical parameters such as pH and temperature [67]. Fabrication of the biosensors involves a multidisciplinary approach where different departments such as chemistry, biology, and engineering come together to develop a sensor for particular application. MNPs play an important role in the fabrication of a biosensors (enzyme-based, tissue-based, immunosensors, DNA biosensors, etc.,) due to their ability to have better sensitivity and a low detection limit [68,69]. MNP based biosensors also have significant advantage when used as biosensors, with the improved sensitivity and limit of detection which helps in detecting a wide range of targets such as DNA/mRNA, proteins, enzyme, drugs, pathogens, and tumor cells [70,71]. MNPs can also be used in multiplexed sensing with different analyses at the same time and can also be used on microfluidic bio sensing

applications [72]. MNP biosensors are mostly used in applications such as biomedicine, clinical diagnostics, pharmaceutical drug development, and genomic, hyperthermia, proteomic, and cancer biology [73,74].

Neural Engineering

Neural engineering is an emerging field dealing with techniques to understand, diagnose, repair, replace, and enhance the neural system (neurons, neural networks and the nervous system) to solve design problem at the interface of neural tissues [75]. MNPs are used in infrared neural stimulation (INS) to generate highly controlled temperature transients in neurons activating to action potentials with greater ease and flexibility [76,77]. MNPs modulate and allow for deeper penetration with the interaction of the magnetic field. MNPs used for neuroscience application are normally of low dimensional nanostructures and interact with subcellular structures effectively [78]. MNPs applied in neuroprotection and neuroregeneration support neural cells by an external magnetic field [79]. These MNPs used in neural engineering work effectively due to their size, high surface-to-volume ratio, multi-functionality, site-specific delivery or targeting, controlled release, and versatility in enabling surface modification [80]. MNPs are used for neuroprotection, neuro regeneration, neuroimaging, and neurosurgery due to their effective interaction with biological systems. MNPs are also used in neuroprotection for neurodegenerative diseases and nerve regeneration after injury [81]. Due to the excellent biocompatibility of the MNPs, they can be used to reduce damage in the neural system having reduced biochemical compounds with the external magnetic field which can be very effective on neural manipulation in the future [82].

Cancer Treatment

MNP based therapy is an emerging biomedical approach with a noninvasive procedure helping patients in subtle approach [83]. MNPs are used for noninvasive imaging of cancer diagnostics and can be therapeutic by using them for targeted drug delivery accounting them for an effective theragnosis approach [84]. MNPs have minimal toxicity in therapeutic approaches when used for targeted drug delivery in cancer treatment [85-87]. MNPs, along with quantum dots or metallic species, create an encapsulation of potential anticancer drugs by iron oxide nano shells [88]. MNP based drug carriers are injected via the blood stream to a tumor location through an externally applied magnetic field. MNPs loaded with drug are delivered at the target site to destroy cancerous cells and tissue [89]. The MNPs are used in hyperthermic treatment using a ferromagnetic or super paramagnetic particle to generate heat in the tumor tissue [90]. MNP based platforms have significant advantages such as active targeting, controlled drug release, sustained drug delivery, and synergistic multimodal treatment [91].

Conclusion and Future Prospects

MNPs have become a popular subject in research due to their numerous biomedical applications. Various MNP coatings have been synthesized from organic to inorganic coatings which each have unique properties and advantages. Co-precipitations are currently the most common method for MNP synthesis being made from aqueous salt solutions and are fitted for biomedical applications such as MRI [92]. Another synthesis technique is microemulsions which synthesize MNPs using two immiscible water and oil phases under the presence of surfactant, and these MNPs have applications in cancer cell therapy. The last method is the sol-gel method in which MNPs, synthesized through a wet approach based upon the hydroxylation and condensation of chemical precursors in solution, can be applied to electrochemical biosensors. Due to MNPs' unique combination of properties, they are especially beneficial in a range of biomedical applications. Their magnetism and nano-dimensions result in their use for MRI contrast, drug delivery, tissue engineering, theragnosis, cell labeling, biosensing, neural engineering, and cancer treatments.

Iron oxide based particles are particular beneficial in MRI contrast, with the ability to detect certain tumors and inflammatory pathologies. MNPs are effective as drug-delivery carriers to treat cancer and neurological disorders due to their hydrophilic qualities and small size. They also have applications in tissue engineering with stem cell replacement therapy and in theragnosis with their magnetic and drug deliverable nature. Cell labelling in stem cells and biosensor capabilities are further implementations of MNPs as they have lower detection limits and improved sensitivity, enhancing detection for pathogens, tumor cells, and other targets. MNPs are applicable in neural engineering, specifically in INS, neuroprotection, neuroimaging, neurosurgery, and neuroregeneration due to a multitude of factors such as their small size and high surface-area-to-volume ratio. Finally, the field of cancer therapies and diagnostics can greatly benefit from MNPs as such procedures are non-invasive and subtle. Further developments in this field will be focused around investigating new synthesis methods, synthesizing new MNPs, and continuing to discover innovative and impactful applications. Sample text inserted for illustration. Replace with article text, including headings where appropriate. Figures and tables can be single- or double-column width as appropriate. During the production process they will be placed at the top or bottom of columns, after they are first cited in the text.

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